SUNDAY POSTER

920 Vascular Biology and Regulation of Blood Flow

Sunday, March 16, 1997, 5:00 p.m.–7:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: 5:00 p.m.–7:00 p.m.

920-83 *Effects of Forearm Exercise Training on* Endothelial Function in Normal Subjects and Patients With Heart Failure

A.J. Bank, R.A. Shammas, P.P. Chuang, K.A. Mullen. *University of Minnesota, Minneapolis, MN, USA*

Endothelium-dependent vasodilation is abnormal in heart failure. This study assessed whether increases in blood flow as a result of forearm exercise training would improve endothelium-dependent vasodilation of forearm resistance vessels. Eleven normal subjects (age 40.4 ± 4.0) and 7 patients with NYHA Class II–III heart failure (age 57.4 ± 5.3) performed handgrip exercise (30% maximum handgrip strength at 30 contractions per minute) of the non-dominant arm for 30 minutes 4 times a week for 4–6 weeks. Forearm blood flow (FBF, ml/min/100 ml forearm volume) was measured by strain-gauge plethysmography before and after exercise training. In the normal subjects the endothelium-dependent vasodilator acetylcholine (10 and 20 μg intra-arterially) increased FBF by 5.8 ± 2.4 and 6.8 ± 3.1 before exercise training. These responses were significantly ($p < 0.05$) increased to 9.2 ± 2.7 and 12.2 ± 3.6 after exercise. The responses to nitroprusside (6.25 and 12.5 μg/min) before exercise (8.2 ± 2.6 and 12.3 ± 3.2) tended to increase (p = NS) after exercise (11.7 ± 4.5 and 16.6 ± 5.1). Peak reactive hyperemia (5 minutes cuff occlusion) increased significantly ($p < 0.05$) from 38.1 ± 5.6 to 47.4 ± 5.6 following exercise. In the heart failure patients, forearm exercise did not significantly increase acetylcholine responses (3.6 ± 1.5 and 5.4 ± 3.6 vs 0.9 ± 0.6 and 6.2 ± 4.0) or peak reactive hyperemia (34.2 ± 5.8 vs 34.2 ± 5.9). Nitroprusside responses tended to increase (p = NS) from 9.6 ± 2.8 and 12.3 ± 3.7 to 14.8 ± 5.9 and 18.4 ± 7.5 after exercise. Basal FBF, and changes in FBF in response to acute forearm exercise and the nitric oxide inhibitor L-NMMA were unchanged in both groups following exercise training. We conclude that a moderate forearm exercise training protocol results in improved forearm resistance vessel endothelium-dependent vasodilation and peak hyperemic vasodilation in normal subjects but not in patients with NYHA Class II–III heart failure.

920-84 Intraday and Day-to-Day Reproducibility of Basal and Post Ischemic Forearm Blood Flow Measurements in Normal Subjects

S. Venkatappa, P. Jadhav, V. Bhaktaram, J. Turner, D. Parker, K. Chandrasekaran, C. Sivaram, U. Thadani. *University of Oklahoma HSC, Oklahoma City, OK, USA*

Forearm Blood Flow Measurements using plethysmography is increasingly being used for evaluation of endothelial function and drug effects. We studied 10 normal non smoker subjects (23–35 y) to investigate intraday and day to day reproducibility of forearm blood flow at basal conditions and at peak hyperemia following prolonged ischemia. Subjects were studied on 4 consecutive days at 8 am after an overnight fast. On two of these days they were made to continue fasting till 10 am when they were studied again. All measurements were made at constant room temp of 23 ± 0.5ºC in the supine position after the subject had rested for a full 15 minutes. Ischemia was induced by complete venous and arterial occlusion at 50 mmHg above systolic blood pressure for 5 minutes and peak hyperemic response was measured within 5 sec of release of the arm cuff by reocclusion of the arm at 40 mmHg. Mean baseline flow for each of the 10 subjects after venous occlusion of the arm at 40 mmHg for 5 sec (cycle of six measurements) fell within the range of 2.8 ± 0.72 ml/min/100 ml with a day to day coefficient of variation of 22.0 ± 9.1%. Mean peak hyperemic response for the group was 40.1 ± 8.4 ml/min/100 ml with a day to day coefficient of variation of 20.2 ± 7.4%. The intra day coefficient of variation for basal and peak hyperemic response for the group was 19.45 ± 7.42% and 16.6 ± 11.8%, respectively. There was no significant difference in intra day and inter day blood pressure values (p = 0.8). We conclude that forearm blood flow measurements using plethysmography varied intra day and from day to day with large individual and group mean coefficients of variation. These findings have important implications when endothelial function and effects of medications are being evaluated using forearm blood flow measurements.

920-85 Single Measurements of Brachial Artery Diameter Significantly Underestimate Endothelial-Dependent Vasomotor Responses

D.M. Herrington, B.L. Werbel, W.A. Riley, D.W. Kitzman, J.G. Warner, L. Fan. *The Bowman Gray School of Medicine, Winston-Salem, NC, USA*

Measurement of brachial artery responses to endothelial vasodilator stimuli using ultrasound is a promising non-invasive method to assess endothelial function. However, most investigators measure arterial diameter at a discrete point in time following a vasodilator stimulus a- strategy not guaranteed to detect the maximum vasodilator response.

To study this, we continuously measured the brachial artery diameter for 2 minutes following a flow stimulus (caused by distal hyperemia) and compared the maximum observed result with the result determined at 1 and 2 minutes post-stimulus.

Results: In 41 separate studies conducted in 15 subjects with established coronary disease, the 1 and 2 minute strategy underestimated the maximum response (expressed as % increase over baseline diameter) by 46% ($p = 0.002$). (Maximum response = 5.17 ± 0.67%; max 1 or 2 minute response = 2.77 ± 0.75%) In 75% of the studies, the 1 and 2 minute strategy yielded a lower response. The correlation between results at 1 minute vs. maximum response was poor ($R^2 = 0.27$).

Conclusion: These data suggest that measurement of brachial artery diameter at discrete points in time following an endothelial-dependent vasomotor stimulus may yield an incomplete assessment of endothelial function.

920-86 Continuous Release of Prostacyclin Contributes to Resting Forearm Blood Flow in Humans

S.J. Duffy, B.T. Tran, G. New, R.W. Harper, I.T. Meredith. *Monash Medical Centre, Melbourne, Victoria, Australia*

Tonic release of nitric oxide contributes to the maintenance of resting tone in the human forearm and coronary circulations, however evidence for a similar role of prostacyclin (PGI_2) is lacking. We examined whether continuous release of PGI_2 contributes to basal forearm blood flow (FBF).

FBF was measured using venous occlusion plethysmography in 17 healthy volunteers (mean age 20.4 ± 2.1 [SD], 6 F, 11 M). Flow was assessed at rest, before and after the endothelial-dependent and independent dilators acetylcholine (ACh, 30 μg/min) and sodium nitroprusside (SNP, 1 μg/min), and with 3 incremental intra-brachial infusions of either the cyclo-oxygenase inhibitor aspirin (ASA) or placebo. Forearm arterial and venous sampling was performed in 4 subjects for 6-keto-PGF1α (the stable metabolite of PGI_2). Levels were measured using a commercially available RIA.

ASA produced a dose-dependent reduction in FBF, resulting in a 34% decrease at the highest dose. FBF at rest and following 1, 3 and 10 mg/min doses was 2.7 ± 0.3, 2.5 ± 0.4, 2.2 ± 0.3 and 1.8 ± 0.3 ml/100 ml of forearm/min, respectively (mean ± SE, $p < 0.001$). Commensurate with this the net forearm production of 6-keto-PGF1α was 76.0 ± 24.3, 20.8 ± 19.0, 24.8 ± 6.2 and 5.0 ± 14.7 pg/100 ml of forearm/min for the respective doses ($p = 0.02$). Analysis of the time course of the effect of ASA (3 mg/min) on FBF revealed a maximal reduction of 22% at 10 mins. Resting FBF measured simultaneously in the contralateral arm was unchanged. Moreover, no time dependent reduction in flow was seen in subjects with vehicle infusion. ASA did not affect the FBF responses to ACh or SNP.

These data suggest that continuous release of PGI_2 plays a role in the maintenance of resting FBF independent of nitric oxide. There appears to be a direct link between the reduction in FBF and PGI_2 production.

920-87 Acute Cyclosporine Ingestion Enhances Endothelium-Mediated Peripheral Vasodilation

A. Beniaminovitz, M.R. Di Tullio, H. Wu, A. Beniaminovitz, I. Titova, L. Mendoza, R. Danziger, S. Katz, S. Homma. *Columbia University, New York, NY, USA*

A postulated mechanism of cyclosporine (Csa) induced hypertension is impairment of endothelial function. While Csa has been shown to decrease endothelium-mediated vasodilation in animals and in vitro human tissue, the effects of Csa on endothelial function in the intact vasculature of humans is unkown. Accordingly, the vasodilatory responses to intra-arterial adminstration of acetylcholine (Ach), an endothelial-mediated vasodilator, and nitroprusside (Ntp), an endothelial-independent vasodilator, were assessed with Doppler ultrasound of the brachial artery. Fifteen normotensive volunteers were studied. Eleven (mean age 29 ± 9 years) underwent testing before and 1 hour after oral adminstration of Csa (5 mg/kg). The remaining 4 (mean age 24 ± 4 years) were tested before and 1 hour after placebo administration. Endothelin-1, 2 and Csa levels were obtained at baseline and at 90 minutes after drug ingestion. Blood pressure was similar in both groups and did not significantly change after Csa ingestion. The vasodilatory responses to Ach